09-14-05

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TRANSMITTAL FORM

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Application Number	10/015,387
Filing Date	DECEMBER 12, 2001
First Named Inventor	KEVIN P. BAKER
Group/Art Unit	1637
Examiner Name	FREDMAN, JEFFREY NORMAN
Total Number of Pages in This Submission: 21	Attorney Docket Number: 39780-2830 P1C54

ENCLOSURES ***(check all that apply)***

- [x] **Fee Transmittal Form**
  - [ ] Fee Attached
- [ ] Response/Amendment
  - [ ] After Final
  - [ ] Version With Markings Showing Changes
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
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- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition Routing Slip (PTO/SB/69) and Accompanying Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, by Assignee to Exclusion of Inventor Under 37 C.F.R. §3.71 With Revocation of Prior Powers
- [ ] Terminal Disclaimer
- [ ] Small Entity Statement
- [ ] Request for Refund
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [x] **Appeal Communication to Group** ***(Appeal Notice, Brief, Reply Brief)***
- [ ] Proprietary Information
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SIGNATURE OF APPLICANT, ATTORNEY OR AGENT

Firm or Individual name	**HELLER EHRMAN LLP**	**BARRIE D. GREENE (Reg. No. 46,740)**	
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Signature	Barrie Greene		
Date	**SEPTEMBER 12, 2005**	Customer Number:	**35489**

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FEE TRANSMITTAL for FY 2005

Effective 10/01/2003. Patent fees are subject to annual revision.

☐ Applicant claims small entity status. See 37 CFR 1.27

TOTAL AMOUNT OF PAYMENT ($) 500.00

Complete if Known	
Application Number	10/015,387
Filing Date	December 12, 2001
First Named Inventor	Kevin P. Baker
Examiner Name	Jeffrey Norman Fredman
Art Unit	1637
Attorney Docket No.	39780-2830 P1C54

METHOD OF PAYMENT *(check all that apply)*

☐ Check ☐ Credit card ☐ Money Order ☐ Other ☐ None

☑ Deposit Account:

Deposit Account Number: 08-1641(39780-2830 P1C54)

Deposit Account Name: HELLER EHRMAN, LLP

The Director is authorized to: *(check all that apply)*

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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1001	300	2001	150	Utility filing fee	
1002	200	2002	100	Design filing fee	
1003	200	2003	100	Plant filing fee	
1004	300	2004	150	Reissue filing fee	
1005	200	2005	100	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

		Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =		X	=
Independent Claims		- 3** =		X	=
Multiple Dependent					=

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
1202	50	2202	25	Claims in excess of 20
1201	200	2201	100	Independent claims in excess of 3
1203	360	2203	180	Multiple dependent claim, if not paid
1204	200	2204	100	** Reissue independent claims over original patent
1205	50	2205	25	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($)

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
1051	130	2051	65	Surcharge - late filing fee or oath	
1052	50	2052	25	Surcharge - late provisional filing fee or cover sheet	
1053	130	1053	130	Non-English specification	
1812	2,520	1812	2,520	For filing a request for *ex parte* reexamination	
1804	920*	1804	920*	Requesting publication of SIR prior to Examiner action	
1805	1,840*	1805	1,840*	Requesting publication of SIR after Examiner action	
1251	120	2251	60	Extension for reply within first month	
1252	450	2252	225	Extension for reply within second month	
1253	1,020	2253	510	Extension for reply within third month	
1254	1,590	2254	795	Extension for reply within fourth month	
1255	2,160	2255	1,080	Extension for reply within fifth month	
1401	500	2401	250	Notice of Appeal	
1402	500	2402	250	Filing a brief in support of an appeal	500.00
1403	1,000	2403	500	Request for oral hearing	
1451	1,510	1451	1,510	Petition to institute a public use proceeding	
1452	500	2452	250	Petition to revive - unavoidable	
1453	1,500	2453	750	Petition to revive - unintentional	
1501	1,400	2501	700	Utility issue fee (or reissue)	
1502	800	2502	400	Design issue fee	
1503	1,100	2503	550	Plant issue fee	
1460	130	1460	130	Petitions to the Commissioner	
1807	50	1807	50	Processing fee under 37 CFR 1.17(q)	
1806	180	1806	180	Submission of Information Disclosure Stmt	
8021	40	8021	40	Recording each patent assignment per property (times number of properties)	
1809	790	2809	395	Filing a submission after final rejection (37 CFR 1.129(a))	
1810	790	2810	395	For each additional invention to be examined (37 CFR 1.129(b))	
1801	790	2801	395	Request for Continued Examination (RCE)	
1802	900	1802	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 500.00

SUBMITTED BY				(Complete *(if applicable)*)	
Name (Print/Type)	Barrie D. Greene	*Registration No. (Attorney/Agent)*	46,740	*Telephone*	(650) 324-7000
Signature				*Date*	September 12, 2005

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: Fredman, Jeffrey Norman
Kevin P. BAKER, et al.	Art Unit: 1637
Application Serial No. 10/015,387	Confirmation No: 9861
Filed: December 12, 2001	Attorney's Docket No. 39780-2830 P1C54
For: **SECRETED AND TRANSMEMBRANE POLYPEPTIDES AND NUCLEIC ACIDS ENCODING THE SAME**	**Customer No. 35489**

EXPRESS MAIL LABEL NO.: EL 976 548 746 US
DATE MAILED: SEPTEMBER 12, 2005

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ON APPEAL TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

APPELLANTS' BRIEF

MAIL STOP APPEAL BRIEF - PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Dear Sir:

On January 18, 2005, the Examiner made a final rejection to pending Claims 28-32 and 44-52. A Notice of Appeal was filed on July 15, 2005.

Appellants hereby appeal to the Board of Patent Appeals and Interferences from the last decision of the Examiner.

The following constitutes Appellants' Brief on Appeal.

1. REAL PARTY IN INTEREST

The real party in interest is Genentech, Inc., South San Francisco, California, by an assignment of the patent application U.S. Serial No. 09/946,374 recorded January 8, 2002, at Reel 012288 and Frame 0504.

2. RELATED APPEALS AND INTERFERENCES

The claims pending in the current application are directed to a polypeptide referred to herein as "PRO1382". There exist two related patent applications, (1) U.S. Serial No. 10/012,754, filed December 7, 2001 (containing claims directed to the PRO1382 polypeptides), and (2) U.S. Serial No. 10/012,064, filed December 7, 2001 (containing claims directed to antibodies that bind the PRO1382 polypeptide). The 10/012,064 application has been allowed. The 10/012,754 application is also under final rejection from the same Examiner and based upon the same outstanding rejection, and appeal of this final rejection is being pursued independently and concurrently herewith.

3. STATUS OF CLAIMS

Claims 28-35, 38-40 and 44-52 are in this application.

Claims 1-27, 36-37 and 41-43 are canceled.

Claims 33-35 and 38-40 are allowed.

Claims 28-32 and 44-52 stand rejected and Appellants appeal the rejection of these claims.

A copy of the rejected claims involved in the present Appeal is provided in the Claims Appendix.

4. STATUS OF AMENDMENTS

There were no amendments to the claims submitted after final rejection. All previous amendments to the claims have been entered.

5. SUMMARY OF CLAIMED SUBJECT MATTER

The invention claimed in the present application is related to isolated nucleic acids e encoding a polypeptide having at least 80%, 85%, 90%, 95%, or 99% amino acid sequence identity to: the amino acid sequence of the polypeptide of SEQ ID NO:220; the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide; the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246, wherein the encoded polypeptide induces proliferation of kidney mesangial cells (Claims 28-32). The invention is further directed to isolated nucleic acids encoding a polypeptide having at least 80%, 85%, 90%, 95%, or 99% amino acid sequence identity to: the amino acid sequence of the polypeptide of SEQ ID NO:220; the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide; the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246, wherein the encoded polypeptide induces proliferation of pancreatic β-cell precursor cells (Claims 48-52). The claims are further directed to vectors comprising the nucleic acids (Claims 44 and 45), and host cell comprising the nucleic acids (Claims 46 and 47).

The full-length PRO1382 polypeptide having the amino acid sequence of SEQ ID NO:220 is described in the specification at, for example, page 18, lines 3-14, page 344, lines 26-32, Example 66, in Figure 126 and in SEQ ID NO:220. The cDNA nucleic acid encoding PRO1382 is described in the specification at, for example, Example 66, in Figure 125 and in SEQ ID NO:219. Page 292, lines 24-28 of the specification provides the description for Figures 125 and 126. PRO polypeptide variants having at least about 80% amino acid sequence identity with a full length PRO polypeptide sequence or a PRO polypeptide sequence lacking the signal peptide are described in the specification at, for example, page 283, lines 2-14. PRO polypeptide variants having at least about 80% amino acid sequence identity with an amino acid sequence encoded by any of the disclosed human protein cDNAs deposited with the ATCC, are described in the specification at, for example, page 283, lines 15-27.

The isolation of cDNA clones encoding PRO1382 of SEQ ID NO:220 is described in Example 66. Methods for isolating PRO cDNA is generally set forth in the specification at, for example page 359, lines 11-34. Methods for selection and transformation of host cells with PRO cDNA is generally set forth in the specification at, for example, page 359, line 36, to page 361, line 24. Methods for selecting a vector are generally set forth in the specification at, for example, page 361, line 26, to page 363, line 25. Finally, Example 145, in the specification at page 509, lines 24-36, sets forth a Mouse Kidney Mesangial Cell Proliferation assay which shows that PRO1382 induces proliferation of mammalian kidney mesangial cells. Example 151 of the specification, at page 512, line 28, to page 513, line 29, sets forth an Induction of Pancreatic β-Cell Precursor Proliferation assay which shows that PRO1382 induces proliferation of pancreatic β-cell precursor cells.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

I. Whether Claims 28-32 and 44-52 satisfy the written description requirement of 35 USC §112, first paragraph.

7. ARGUMENT

Summary of the Arguments

Claims 28-32 and 44-52 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking adequate written description for the recited nucleic acids encoding variants of the PRO1382 polypeptide (SEQ ID NO:220). Appellants note that the claims recite structural features, namely, 80% sequence identity to SEQ ID NO:220, which are common to the genus. The specification provides detailed guidance as to how to identify the recited variants of SEQ ID NO:220, including methods for determining percent identity between two amino acid sequences, as well as listings of exemplary and preferred sequence substitutions. The genus of polypeptides encoded by the claimed nucleic acids is further defined by having a specific functional activity, namely, that the polypeptide induces proliferation of kidney mesangial cells, or induces proliferation of pancreatic β-cell precursor cells. Examples 145 and 151 of the present application provides step-by-step guidelines and protocols for the mouse kidney mesangial cell proliferation assay and the pancreatic β-cell precursor proliferation assay.

By following the disclosure in the specification, one skilled in the art can easily test whether a variant PRO1382 protein induces proliferation of kidney mesangial cells, or induces proliferation of pancreatic β-cell precursor cells. Thus one of skill in the art could identify whether a variant PRO1382 sequence falls within the parameters of the claimed invention. Accordingly, a description of the claimed genus has been achieved by the recitation of both structural and functional characteristics.

The Examiner's assertion that the claimed genus of nucleic acids includes 4^{120} sequences is therefore incorrect, because the claimed genus includes only those nucleic acids encoding polypeptide variants having at least 80% identity to SEQ ID NO:220 which also have a specified activity, that is, inducing proliferation of kidney mesangial cells, or inducing proliferation of pancreatic β-cell precursor cells. Once the additional functional limitations are included, the genus is limited to a size where the demonstrated species suffices to represent the genus.

The Examiner has asserted that the recited function allegedly "provides absolutely no guidance or information regarding the structure and does not limit the structure in even the smallest or most miniscule possible way." (Page 7 of the Office Action mailed January 15, 2005). The recited functional limitations clearly limit the structure of the variants in the obvious sense that a protein lacking any structural similarity with SEQ ID NO:220 would not be expected to conserve the same function. It is not necessary that the functional limitation be directly linked to structure, because the claims already provide a structural limitation, in requiring that the claimed variants have at least 80% amino acid sequence identity to SEQ ID NO:220. Structurally unrelated polypeptides having a similar function would not be encompassed by claims requiring at least 80% amino acid sequence identity to SEQ ID NO:220.

The Examiner has further asserted that the Written Description Guidelines "require a structure function relationship." To the contrary, Example 14 of the Synopsis of Application of Written Description Guidelines issued by the U.S. Patent Office clearly states that protein variants meet the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins are routine in the art, (2) the specification provides an assay for detecting the functional activity of the protein and (3) the variant proteins possess the specified functional activity and a defined

degree of sequence identity to the reference sequence. Accordingly, the claimed variants meet the standards set forth in the Written Description Guidelines.

These arguments are discussed in further detail below.

Claims 28-32 and 44-52 Satisfy the Written Description Requirement of 35 U.S.C. §112, First Paragraph

Claims 28-32 and 44-52 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner has asserted that "the genus includes variants for which no written description is provided in the specification. This large genus is represented in the specification by only the particularly named SEQ ID NO:219. Thus, applicant has express possession of only one particular nucleic acid sequence in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains." (Page 3 of the Office Action mailed January 15, 2005).

Appellants submit, for the reasons set forth below, that the specification provides an adequate written description for the claimed PRO1382 nucleic acid variants.

A. The Legal Test for Written Description

The well-established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph is "whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language."[1] [2] The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis.[3] The factual determination in a written

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[1] *In re Kàslow*, 707 F.2d 1366, 1374, 212 U.S.P.Q. 1089, 1096 (Fed. Cir. 1983).

[2] *See also Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116 (Fed. Cir. 1991).

[3] *See e.g., Vas-Cath*, 935 F.2d at 1563; 19 U.S.P.Q.2d at 1116.

description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. [4] [5]

In *Environmental Designs, Ltd. v. Union Oil Co.*,[6] , the Federal Circuit held, "Factors that may be considered in determining level of ordinary skill in the art include (1) the educational level of the inventor; (2) type of problems encountered in the art; (3) prior art solutions to those problems; (4) rapidity with which innovations are made; (5) sophistication of the technology; and (6) educational level of active workers in the field." (Emphasis added).[7] Further, The "hypothetical 'person having ordinary skill in the art' to which the claimed subject matter pertains would, of necessity have the capability of understanding the scientific and engineering principles applicable to the pertinent art."[8] [9]

B. The Disclosure Provides Sufficient Written Description for the Claimed Invention

Appellants respectfully submit that the instant specification evidences the actual reduction to practice of a full-length PRO1382 polypeptide of SEQ ID NO:220, with or without its signal sequence. The Examiner has acknowledged that nucleic acids encoding a polypeptide comprising the sequence set forth in SEQ ID NO:220 (as in Claims 33-35) meets the written description provision of 35 U.S.C. §112, first paragraph. Thus, the genus of nucleic acids that encode polypeptides with at least 80% sequence identity to SEQ ID NO:220, which possess the functional property of either inducing proliferation of kidney mesangial cells, or inducing proliferation of pancreatic β-cell precursor cells, would meet the requirement of 35 U.S.C. §112, first paragraph, as providing adequate written description.

Appellants have provided native PRO sequence SEQ ID NO:220, and SEQ ID NO:219 which encodes it. The present application also describes methods for identifying proteins which

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[4] *Union Oil v. Atlantic Richfield Co.*, 208 F.2d 989, 996 (Fed. Cir. 2000).

[5] *See also* M.P.E.P. §2163 II(A).

[6] 713 F.2d 693, 696, 218 U.S.P.Q. 865, 868 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1043 (1984).

[7] *See also* M.P.E.P. §2141.03.

[8] *Ex parte Hiyamizu*, 10 U.S.P.Q.2d 1393, 1394 (Bd. Pat. App. & Inter. 1988) (emphasis added).

[9] See *also* M.P.E.P. §2141.03.

induce proliferation of kidney mesangial cells or pancreatic β-cell precursor cells. Example 145 of the present application provides step-by-step guidelines and protocols for the mouse kidney mesangial cell proliferation assay. By following the disclosure in the specification, one skilled in the art can easily test whether a polypeptide encoded by a variant PRO1382 nucleic acid induces proliferation of kidney mesangial cells. Example 151 of the present application provides step-by-step guidelines and protocols for the pancreatic β-cell precursor proliferation assay. By following the disclosure in the specification, one skilled in the art can easily test whether a polypeptide encoded by a variant PRO1382 nucleic acid induces proliferation of pancreatic β-cell precursor cells.

The specification also describes methods for the determination of percent identity between two amino acid sequences. (See page 302, line 4 to page 305, line 4). In fact, the specification teaches specific parameters to be associated with the term "percent identity" as applied to the present invention. The specification further provides detailed guidance as to changes that may be made to a PRO polypeptide without adversely affecting its activity (page 354, line 30 to page 357, line 7). This guidance includes a listing of exemplary and preferred substitutions for each of the twenty naturally occurring amino acids (Table 6, page 356). Accordingly, one of skill in the art could identify whether a variant PRO1382 sequence falls within the parameters of the claimed invention. Once such an amino acid sequence was identified, the specification sets forth methods for making the amino acid sequences (see page 354, line 30 to page 358, line 34) and methods of preparing the PRO polypeptides (see page 358, line 35 and onward). Methods of isolating nucleic acid sequences encoding PRO polypeptides and polypeptide variants are described in the specification at, for example, page 364, lines 25-38. Accordingly, one of skill in the art could identify whether a variant PRO1382 nucleic acid sequence falls within the parameters of the claimed invention.

Accordingly, the specification provides adequate written description for nucleic acids encoding polypeptides having at least 80% identity to SEQ ID NO:220 wherein the encoded polypeptide induces proliferation of kidney mesangial cells, or induces proliferation of pancreatic β-cell precursor cells.

The Examiner has asserted,

> It is the absence of any real structure function relationship and the absence of a representative number of species which supports the conclusion that there is insufficient descriptive support for the current claims. This argument rests on several grounds. First, the single sequence that is actually described is not representative of the genus of any sequence which hybridizes under the claimed conditions. Second, the claims entirely lack a structure function relationship since the function given has no ability to limit the genus of polypeptides. Third, the claim encompasses species other than human.

(Page 6 of the Office Action mailed January 15, 2005).

Appellants respectfully point out that the claims are not directed to hybridizing sequences. The claims recite nucleic acids defined as encoding polypeptides having a specified degree of sequence identity to SEQ ID NO:220, as well as a specified function. Thus the Examiner's first point is not relevant to the claims at issue. Regarding the second point, Appellants respectfully note that the claims are directed to nucleic acids, not polypeptides.

The Examiner has further asserted that the genus of polypeptides encoded by the claimed nucleic acids allegedly "represents every possible variation which could occur in SEQ ID NO:220, that has 80% identity," and that this genus includes 4^{120} sequences. This statement is incorrect. The claimed genus of nucleic acids includes only those encoding polypeptide variants having at least 80% identity to SEQ ID NO:220 which also have a specified activity, that is, inducing proliferation of kidney mesangial cells, or inducing proliferation of pancreatic β-cell precursor cells.

The Examiner has asserted that the recited function allegedly "provides absolutely no guidance or information regarding the structure and does not limit the structure in even the smallest or most miniscule possible way." (Page 7 of the Office Action mailed January 15, 2005). Appellants respectfully disagree. First, the functional limitation clearly limits the structure of the variants in the obvious sense that a protein lacking any structural similarity with SEQ ID NO:220 would not be expected to conserve the same function. Second, it is not necessary that the functional limitation be directly linked to structure, because the claims already provide a structural limitation, in requiring that the polypeptide variants encoded by the claimed nucleic acids have at least 80% amino acid sequence identity to SEQ ID NO:220. Appellants recognize that there may be polypeptides that induce proliferation of kidney mesangial cells or pancreatic β-cell precursor cells through mechanisms unrelated to those of PRO1382, and thus do

not resemble PRO1382 in structure. These structurally unrelated polypeptides, however, would not be encompassed by claims requiring at least 80% amino acid sequence identity to SEQ ID NO:220. Appellants claim only those nucleic acids which encode proteins meeting both limitations of the claims, structural and functional. Given the structural limitation, the additional functional limitation clearly acts to further define the claimed genus.

As the Examiner has pointed out, the size of the genus is a central issue, because if the genus were smaller, a written description issue would be less likely, since the examples would be more representative of the genus. (Page 8 of the Office Action mailed January 15, 2004). As discussed above, the claims do not encompass anywhere near the extremely large number of species stated in the Office Action, because the Examiner's calculation is based solely upon the structural limitation of at least 80% sequence identity. Once the additional functional limitations are included, the genus is limited to a size where the demonstrated species suffices to represent the genus.

The Office Action appears to interpret the quoted statement in *The Regents of the University of California v. Eli Lilly and Co.* (43 U.S.P.Q.2d 1398 (Fed. Cir. 1997)) that a definition by function does not suffice to define a genus, as meaning that functional limitations are without significance, and may be ignored. (See page 4 of the Office Action mailed January 15, 2005). Appellants do not, as in *Lilly*, claim nucleic acid sequences solely by their functional utility or expected result. Rather, the recited functional limitations serve to supplement the recited structural limitations. Furthermore, the recited functional limitations do not set forth only a "useful result," but the features which achieve that result, as required by *Lilly*. The claims do not recite proteins of unspecified characteristics that are useful in treating kidney diseases or disorders associated with decreased β-cell function, such as diabetes mellitus. The claims recite proteins which have a specific activity, inducing proliferation of kidney mesangial cells or pancreatic β-cell precursor cells, which can be measured by assays disclosed within the specification.

The Office Action also appears to argue that Appellants must provide a single limitation that describes both structural and functional attributes together, asserting that the Written Description Guidelines "require a structure function relationship." (Page 9 of the Office Action mailed January 15, 2004).

The Office Action fails to explain where this requirement is found in the Written Description Guidelines. Appellants respectfully note that there is no "structure function relationship" provided in Example 9 of the Written Description Guidlines. Rather, the claims in Example 9 resemble the instant claims in providing both a structural limitation (given that nucleic acids which hybridize to the reference sequence under stringent conditions would share significant sequence identity), together with a separate functional limitation, that the encoded polypeptides have adenylate cyclase activity. Since the structural limitation pertains to the nucleic acids, while the functional limitation pertains to the encoded polypeptides, it is difficult to see how there can be a direct structure function relationship.

The Board's attention is respectfully directed to Example 14 of the Synopsis of Application of Written Description Guidelines issued by the U.S. Patent Office, which clearly states that protein variants meet the requirements of 35 U.S.C. §112, first paragraph, as providing adequate written description for the claimed invention even if the specification contemplates but does not exemplify variants of the protein if (1) the procedures for making such variant proteins are routine in the art, (2) the specification provides an assay for detecting the functional activity of the protein and (3) the variant proteins possess the specified functional activity and at least 95% sequence identity to the reference sequence.

As discussed above, the procedures for making the claimed variant proteins are well known in the art and described in the specification. The specification also provides assays, shown in Example 145 and Example 151, for detecting the recited functional activity of the claimed variants. Finally, the claimed variant proteins possess both the specified functional activity and a defined degree of sequence identity to the reference sequence, SEQ ID NO:220. Accordingly, the recited variants, and the claimed nucleic acids that encode them, meet the standards set forth in the Written Description Guidelines.

Finally, the Examiner has asserted that Appellants' claims suffer from the same flaw as in *Lilly*, since the instant claims would allegedly encompass sequences from other species. Appellants respectfully point out that the issue is not whether the claims encompass sequences from other species, but whether the claimed sequences are adequately described. The assumption that any claim which covers sequences from another species is automatically too broad would lead to the perverse result that a genus that was more highly conserved across species would be

harder to provide written description for, since any given degree of sequence identity would be more likely to include the variants from other species.

As discussed above, the claimed sequences are defined both by a structural limitation (encoding proteins having at least 80% amino acid sequence identity to a described reference sequence), and by a functional limitation, (encoding proteins having a specific biological activity, as measured by specific, disclosed assays). This biological activity, coupled with a well defined, and relatively high degree of sequence identity, sufficiently defines the claimed genus, such that one skilled in the art would readily recognize that the Appellants were in the possession of the invention claimed at the effective filing date of this application.

CONCLUSION

For the reasons given above, Appellants submit that Claims 28-32 and 44-52 meet the written description requirement of 35 USC §112, first paragraph.

Accordingly, reversal of the rejection of claims 28-32 and 44-52 under 35 § U.S.C. 112, first paragraph, is respectfully requested.

Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2830 P1C54**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: September 12, 2005

By: _____
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8. CLAIMS APPENDIX

Claims on Appeal

28. An isolated nucleic acid encoding a polypeptide having at least 80% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of kidney mesangial cells.

29. The isolated nucleic acid of Claim 28 encoding a polypeptide having at least 85% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of kidney mesangial cells.

30. The isolated nucleic acid of Claim 28 encoding a polypeptide having at least 90% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of kidney mesangial cells.

31. The isolated nucleic acid of Claim 28 encoding a polypeptide having at least 95% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of kidney mesangial cells.

32. The isolated nucleic acid of Claim 28 encoding a polypeptide having at least 99% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of kidney mesangial cells.

33. An isolated nucleic acid comprising:

(a) a nucleic acid sequence encoding the polypeptide of SEQ ID NO:220;

(b) a nucleic acid sequence encoding the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the nucleic acid sequence shown in Figure 125 (SEQ ID NO:219);

(d) the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(e) the full-length coding sequence of the cDNA deposited under ATCC accession number 203246.

34. The isolated nucleic acid of Claim 33 comprising a nucleic acid sequence encoding the polypeptide of SEQ ID NO:220.

35. The isolated nucleic acid of Claim 33 comprising a nucleic acid sequence encoding the polypeptide of SEQ ID NO:220, lacking its associated signal peptide.

38. The isolated nucleic acid of Claim 33 comprising the nucleic acid sequence of SEQ ID NO:219.

39. The isolated nucleic acid of Claim 33 comprising the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219.

40. The isolated nucleic acid of Claim 33 comprising the full-length coding sequence of the cDNA deposited under ATCC accession number 203246.

44. A vector comprising the nucleic acid of Claim 28 or 48.

45. The vector of Claim 44, wherein said nucleic acid is operably linked to control sequences recognized by a host cell transformed with the vector.

46. A host cell comprising the vector of Claim 44.

47. The host cell of Claim 46, wherein said cell is a CHO cell, an *E. coli* or a yeast cell.

48. An isolated nucleic acid encoding a polypeptide having at least 80% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of pancreatic β-cell precursor cells.

49. The isolated nucleic acid of Claim 48 encoding a polypeptide having at least 85% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of pancreatic β-cell precursor cells.

50. The isolated nucleic acid of Claim 48 encoding a polypeptide having at least 90% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of pancreatic β-cell precursor cells.

51. The isolated nucleic acid of Claim 48 encoding a polypeptide having at least 95% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of pancreatic β-cell precursor cells.

52. The isolated nucleic acid of Claim 48 encoding a polypeptide having at least 99% sequence identity to:

(a) the amino acid sequence of the polypeptide of SEQ ID NO:220;

(b) the amino acid sequence of the polypeptide of SEQ ID NO:220, lacking its associated signal peptide;

(c) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the nucleic acid sequence of SEQ ID NO:219; or

(d) the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposited under ATCC accession number 203246,

wherein the encoded polypeptide induces proliferation of pancreatic β-cell precursor cells.